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First step in immunotherapies era: any hope to cure or not; review article

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SUMMARY

Immunotherapy is the standard treatment for certain types of cancer that have spread such as melanoma. It aids the immune system to recognize and attack cancer cells. Unlike other forms of treatment that produce harsh side effects such as chemotherapy; immunotherapy causes less harm as it uses the patient's immune system and is a milder form of treatment. Thus, immunotherapy is a more preferable way in the treatment of cancer such, especially ovary, lung, breast, or renal so as to ensure recovery with fewer difficulties.

Normally, the human body has natural capabilities to detect and eradicate abnormal cells that could evolve into cancer. Some cancer cells are however capable of producing signals that blind the immune system from detecting them or by changing themselves so they are unrecognizable. Immunotherapy thus looks to restore and sharpen the ability of the immune system to encounter these problems efficiently. Such therapies work in two major ways. They invigorate parts of the immune system so they can work better and also neutralize signals from cancer cells which inhibit the immune system.

Key words: immunotherapies, chemotherapy, T-cell therapy, melanoma

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INTRODUCTION

In recent years, Immunotherapy has developed as an important alternative to other cancer treatment methods such as chemotherapy and target therapy. While immunotherapy is a pronounced method to fight cancer, it has not been adopted extensively because different patients have varied immune systems which are affected by different factors. Immune systems are impacted by age, diet and environmental exposure, thus it's prudent to formulate different and targeted therapies for different individuals. The research findings are supported by data and information provided by the SEER database. Additionally, more advanced research is required to reduce the reported cases of failure by the cancerous tumor to respond to immunotherapy.

Types of Immunotherapy

There are about four types of immunotherapy treatments in existence. These are (1): Monoclonal antibodies /tumor-agnostic therapies, (2): Oncolytic virus therapy, (3): Cancer vaccines, and (4): T-cell therapy.

Monoclonal antibodies

While monoclonal antibodies are developed in the laboratory for use as intended therapy to block abnormal proteins in cancerous cells, they may also serve as immunotherapy. This is where monoclonal antibodies affix themselves to specific proteins on cancerous cells in order to flag them to the immune system for faster destruction.

Oncolytic virus therapy

In oncolytic virus therapy, doctors introduce the genetically modified virus to the cancer tumor through injection. The virus penetrates the cancerous cells and duplicates itself rapidly. The cell then bursts and releases antigens while it dies. It in turn alerts the person's immune system to all cancer cells attached with those antigens for destruction. It is important to note that the virus does not enter healthy cells.

PVSRIPO is a genetically recombinant, non-pathogenic poliovirus: rhinovirus chimera with a tumor-specific conditional replication phenotype [1, 2].

The first-in-human PVSRIPO clinical trial was initiated at the Preston Robert Tisch Brain Tumour center at Duke University Medical center in early 2012 as a phase I trial in patients with histologically confirmed recurrent World Health Organization grade IV malignant glioma (GBM or gliosarcoma).

PVSRIPO was infused intratumorally via convection-enhanced delivery (Figure 1).

Only one dose-limiting toxicity was observed: an intracranial hemorrhage at the time of catheter removal. Adverse events observed so far have been related to secondary inflammatory response and prolonged corticosteroid use. Initial worsening on MRI suggestive of inflammatory toxicity seems to improve over time at lower dose levels. As of the last update, three patients were disease-free more than 23, 35, and 36 months after PVSRIPO infusion [3].

Cancer vaccines

Cancer vaccines are also used to assist the body fight cancer. They expose the immune system to an antigen and trigger it to identify and destroy that antigen and related materials. Several trials were carried out for the role of a cancer vaccine for cancer patients (Figure 2).

T-cell therapy

A type of treatment in which a patient's T cells (a type of immune system cell) is changed in the laboratory so they will attack cancer cells. T cells are taken from a patient's blood. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added in the laboratory. The special receptor is called a Chimeric Antigen Receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion. CAR T-cell therapy is being studied in the treatment of some types of cancer. Also called chimeric antigen receptor T-cell therapy.

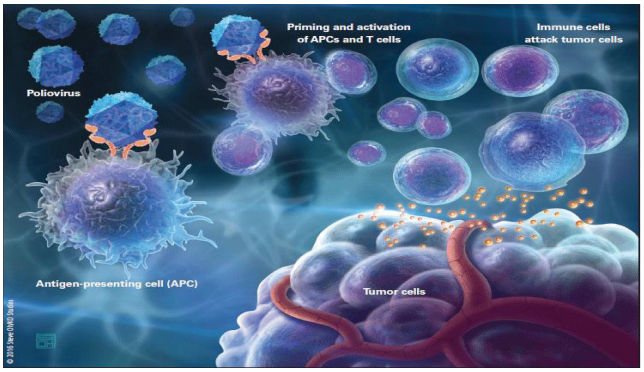

Fig. 1. Recruitment of effector adaptive immune response against tumour after exposure to PVSRIPO

Type	Agent	Authors	Phase
Vaccines			
Peptide	Rindopepimut	Sampson[28]	II
		Schuster[29]	II
		Reardon[30]	II
	IMA950	Halford[33]	I
Heat shock protein	HSPPC-96	Bloch[44]	II
Dendritic cell	DCVax	Northwest Biotherapeutics[60]	II
	ICT-107	Wen[62]	II
	αDC1	Okada[51]	I/II
	DC CMV	Vlahovic[63] Mitchell[64]	I I
Oncolytic viruses			
	DNX-2401	Lang[65]	I
	G207	Markert[66]	I
	H-1PV	Geletneky[67]	I/IIa
	PVSRIPO	Desjardins[69]	I

αDC1 = α-type-1-polarized dendritic cell; DC CMV = dendritic cell cytomegalovirus; H-1PV = oncolytic parvovirus H-1; HSPPC-96 = heat shock protein protein complex-96; PVSRIPO = poliovirus:rhinovirus chimera with a tumor-specific conditional replication phenotype.

Fig. 2. Vaccine and oncolytic virus trials

Cancer immune editing

Cancer immune editing is a complex process that explains the interaction between host defenses and neoplastic condition that could either promote or suppress the growth of cancerous cells. Cancer immune editing has previously been interpreted as a three-phase process which involves eradication, balance, and escape (Figure 3).

(A) The eradication/elimination phase: It is considered as the initial phase from which the programmed death of tumor cells takes place. The elimination phase relies heavily on the innate and adaptive immune mechanisms in the body.

(B) The equilibrium phase: It is the stage acts upon the surviving cancer cells. In the second stage, the growth of surviving cancerous cells is highly restricted.

(C) The escape phase: It is characterized with clinically apparent tumors due to the invasion of immune-surveillance by the cancer cells that creates resistant clones.

The antitumor activities can be held by different types of immune cells with T cell holding a significant level of attention. A considerable number of co-stimulatory signals are required to meditate the T-cell cytotoxicity. Some of the essential activation signals include activities of the CD28 antigens and interactions on the surfaces of antigen-presenting cells. Notably, the current success in the immunotherapeutic solutions for solid tumors can be linked to recent advancement in immune-modulation of antibodies. Such antibodies are then directed towards the crucial checkpoints including the PD-1 [4].

The therapeutic vaccines have also proved to be effective in the induction of the host immune system as well as providing long-term responses in recognition of tumor antigens. The therapeutic vaccines include the antigen-specific immunotherapy and tumor cell therapies. The melanoma-associated antigen-A3 is an example of a popular antigen-specific immunotherapy vaccine. Immunotherapy is therefore identified as a critical component for the development of future treatment for lung cancer.

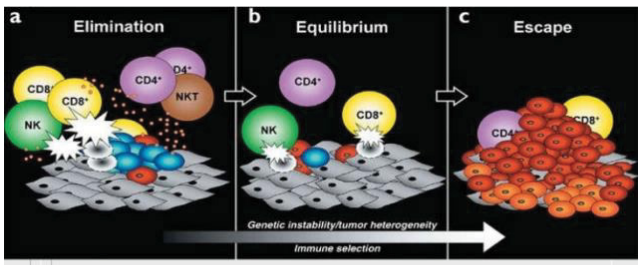

Fig. 3. Immunoediting steps of cancer cells

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